Summary Report of the JECFA/JMPR Working Group on Residue Definition

3-7 December 2018

WHO Headquarter, Geneva (Switzerland)

Background and introduction

Following the recommendations of the Joint FAO/WHO Expert Committee on Food Additives (JECFA) (FAO/WHO, 2016) and of the Joint FAO/WHO Meeting on Pesticide Residues (JMPR) (FAO/WHO, 2014; FAO/WHO, 2015), an expert working group on methodology applied by JECFA and JMPR to estimate chronic dietary exposure was established jointly by FAO and WHO. The working group was formed to address the issue of how to estimate less-than-lifetime exposure and dietary exposure to residues of substances used as both veterinary drugs and pesticides. One recommendation of the working group was for JECFA and JMPR to pursue harmonisation of their residue definitions to facilitate exposure assessment of dual use compounds (and subsequently facilitate harmonisation of enforcement strategies).

Based on this recommendation, a working group of JECFA and JMPR experts was formed by FAO/WHO and a meeting was convened on 3-7 December 2018 in conjunction with the meeting of the OECD working group on the revision of the guidance document for residue definition.

Conclusions and recommendations

The conclusions and recommendations of the JECFA/JMPR working group on residue definition are summarized hereafter.

- For dual use compounds, the working group recommends to continue using the most refined approach based on data submitted by the sponsors to determine the relevant residues of toxicological concern. While this approach is routinely used by JMPR, JECFA has used this approach only when such data were available. In cases where the relevant toxicological data are not available in the veterinary drug dossier, the sponsor is encouraged to access such data (i.e., buy it or obtain right of reference from the sponsor of the pesticide dossier). It was noted that the JMPR report or monograph is typically insufficient for JECFA’s evaluation, as it only provides a summary of the data (not the raw data itself). In the absence of the data necessary for a more refined residue
of concern, JECFA will continue to use the Total Radioactive Residue (TRR) method which is less accurate but more conservative than the JMPR approach.

- With respect to metabolite identification and evaluation for animal commodities: as described in VICH GL46¹, a threshold for identifying metabolites of potential concern would be:
  - ≥ 100 μg/kg
  - OR: ≥ 10% of TRR, in the sample collected at the earliest sample time.

The working group recommends that JMPR follows a similar approach for identifying metabolites of concern in animal commodities, in parallel with existing JMPR methods for deriving thresholds of metabolite identification.

It was reiterated that JECFA and JMPR expect that a majority of the Total Residue be structurally identified. If this is not feasible, the sponsor is expected to provide a scientific explanation.

The working group recommends that a “Total Residue” approach (e.g. TRR) is added to the OECD guidelines to cover cases where data are insufficient to enable individual metabolite assessment.

- The working group recommends that for the assessment of bound residues, the analytical extraction methods used to prove that the residue is truly “bound”, be compared between JMPR and JECFA. While the exact extraction protocol does not need to be specified (as this will depend on the nature of the compound and the matrix), some general extraction procedures should be performed (e.g., acid, base, enzymatic digestion, etc.).

- The working group noted that CCPR and CCRVDF should harmonize their definitions of “muscle” and “fat”. The working group recommends that the JMPR secretariat raise this issue at the next CCPR in 2019 (i.e., CCPR consider adopting the CCRVDF definitions).

- The working group confirms that residue definitions of the marker residue both at JECFA and JMPR should include any relevant instructions necessary for the analysis (e.g., hydrolysis of conjugates).

¹ Studies to evaluate the metabolism and residue kinetics of veterinary drugs in food-producing animals: Metabolism study to determine the quantity and identify the nature of residues
VICH GL46 (MRK) - February 2011 - Implemented in February 2012 - https://vichsec.org/component/attachments/attachments/312.html?task=download
• The working group also re-affirms JECFA’s previous conclusion that, when available, information regarding the effect of food processing on residues should be considered. It was also noted that for dual-use substances, JECFA should consider any data from JMPR monographs regarding effects of food processing on residues.

• The working group recommends to the WHO/JECFA secretariat that the guidance documents for monographers be updated regarding approaches for metabolite assessment, including Threshold of Toxicological Concern (TTC).

• The working group recommends that JECFA and JMPR explore what would be the minimum value or level (on a % or µg/kg basis) of a metabolite resulting in a significant impact on the exposure assessment.

References


List of participants

JECCA/JMPR experts of the working group

- Alan Boobis, Imperial College London, United Kingdom
- Alan Chicoine, University of Saskatchewan, Canada
- Dugald Maclachlan, Department of Agriculture and Water Resources, Australia
- Holly Erdely, FDA, United States of America
- Johan Schefferlie, Medicines Evaluation Board Agency, the Netherlands
- Michael Doherty, EPA, United States of America
- Pascal Sanders, ANSES, France
- Shah Pv, EPA, United States of America
- Stefan Scheid, BVL, Germany
- Trijntje van der Velde-Koerts, RIVM, Netherlands

Joint FAO/WHO Secretariat

- Vittorio Fattori, FAO
- Markus Lipp, FAO
- Soren Madsen, WHO
- Philippe Verger, WHO
- YongZhen Yang, FAO